What will surgical coronary revascularization look like in 25 years?

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Abstract: PURPOSE OF REVIEW Coronary artery bypass grafting evolved in incremental but significant steps since its introduction. Here, we provide an update on operative techniques, choice of conduits, patient selection/decision-making and primary and secondary prevention measures with potential of influencing the future of coronary artery bypass grafting (CABG) surgery. RECENT FINDINGS Associated mortality of off-pump CABG (OPCAB) procedures performed in high-volume OPCAB centers (164 cases per year) and by experienced surgeons (48 cases per year) was reduced compared with on-pump CABG with two or more grafts suggesting a volume-based dependency of outcomes in CABG procedures with high-technical complexity. Ten-year results from the recent Arterial Revascularization Trial showed no significant between-group difference for the primary and secondary outcome. Total arterial revascularization using composite bilateral internal mammary artery-Y-conduits through a limited access mini-thoracotomy was not only shown to be feasible but a safe and reproducible procedure with excellent midterm outcomes. The most recent Randomized Trial of Endoscopic or Open Vein-Graft Harvesting for Coronary-Artery Bypass (REGROUP) trial demonstrated no significant difference between open vein-graft harvesting and endoscopic vein-graft harvesting in the occurrence of major adverse cardiac events. SUMMARY Adherence to the most recent guidelines on myocardial revascularization is a key component for providing state-of the CABG surgery. Trends to lesser invasiveness in surgical coronary revascularization will gain momentum and is expected - with further improvements - to be the mainstay of future surgical coronary revascularization strategies.

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What will surgical coronary revascularization look like in 25 years?

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Purpose of review
Coronary artery bypass grafting evolved in incremental but significant steps since its introduction. Here, we provide an update on operative techniques, choice of conduits, patient selection/decision-making and primary and secondary prevention measures with potential of influencing the future of coronary artery bypass grafting (CABG) surgery.

Recent findings
Associated mortality of off-pump CABG (OPCAB) procedures performed in high-volume OPCAB centers (≥164 cases per year) and by experienced surgeons (≥48 cases per year) was reduced compared with on-pump CABG with two or more grafts suggesting a volume-based dependency of outcomes in CABG procedures with high-technical complexity. Ten-year results from the recent Arterial Revascularization Trial showed no significant between-group difference for the primary and secondary outcome. Total arterial revascularization using composite bilateral internal mammary artery-Y-conduits through a limited access mini-thoracotomy was not only shown to be feasible but a safe and reproducible procedure with excellent midterm outcomes. The most recent Randomized Trial of Endoscopic or Open Vein-Graft Harvesting for Coronary-Artery Bypass (REGROUP) trial demonstrated no significant difference between open vein-graft harvesting and endoscopic vein-graft harvesting in the occurrence of major adverse cardiac events.

Summary
Adherence to the most recent guidelines on myocardial revascularization is a key component for providing state-of the CABG surgery. Trends to lesser invasiveness in surgical coronary revascularization will gain momentum and is expected – with further improvements – to be the mainstay of future surgical coronary revascularization strategies.

Keywords
coronary artery bypass grafting, coronary artery disease, coronary computed tomography angiography, minimally invasive direct coronary artery bypass grafting, multiarterial grafting, off-pump coronary artery bypass, totally endoscopic coronary bypass grafting

INTRODUCTION

Today, coronary artery disease (CAD) is the most common cause of mortality and morbidity in developed countries [1]. In the subsequent years and decades after Sabiston performed the first, nonmechanical, sutured anastomosis of a saphenous vein graft to the right coronary artery to be the first coronary artery bypass grafting (CABG) procedure and remains today the standard surgical revascularization treatment in patients with complex multivessel CAD and/or left main disease, diabetes, or reduced left ventricular function [2–6]. Substantial efforts have been invested in operative techniques, choice of conduits, patient selection/decision-making and primary and secondary prevention to address the invasiveness and the safety of CABG procedures while improving short-term and long-term outcomes throughout the past decades [7].

The current review aims to provide an overview of recent developments with the potential of

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KEY POINTS

- CABG remains the standard surgical revascularization treatment in patients with complex multivessel CAD and/or left main disease, diabetes, or reduced left ventricular function.
- CABG surgery with intense structured training in highly dedicated programs needs to be implemented as a subspecialty within cardiac surgery.
- New technological developments in robotic CABG surgery may provide broader applicability in selected patient populations.
- While further evidence on the merits of multiarterial grafting is necessary, significant efforts are being invested to optimize patency outcomes of saphenous vein grafts.
- New diagnostic tools such as coronary computed tomography angiography, FFR instantaneous wave-free ratio and fusion imaging techniques involving anatomical and functional modalities may in future impact the patient selection and decision making for a patient-tailored approach.

influencing the fate of surgical coronary revascularization in the upcoming decades.

MARKET SHARE OUTLOOK

Despite technological advancements of percutaneous coronary intervention (PCI) in the recent years, today with approximately 371 000 procedures per year in the United States and 40–60 procedures per 100 000 inhabitants in Europe, the utilization of CABG worldwide is again on the rise as a consequence of large-scale trials demonstrating the survival benefits associated with CABG [8–10]. Although the incidence has decreased over the past decade, CAD remains the leading cause of mortality worldwide [1]. However, a further increase due to stress, unhealthy diets, obesity reaching epidemic proportions, and sedentary lifestyle together with the aging population is likely in the coming decades. Accordingly, a further growth of the global CABG market is highly expected for the upcoming decades.

GUIDELINE ADHERENCE AND IMPACT OF PUBLIC REPORTING

Clinical practice guidelines summarizing and evaluating all available evidence aim to assist physicians in selecting the best management strategies for an individual patient thus improving the quality of outcomes. As such, adherence to the most recent 2018 ESC/EACTS Guidelines on myocardial revascularization is a key component for providing state-of-the-art CABG surgery. Public performance reporting (PPR) and patient-reported outcomes as a means of performance measure aim to further improve the quality of care and informed patient choice and is being increasingly endorsed in modern CABG surgery practice in the United States and Europe [11]. A recent systematic review and meta-analysis of the impact of PPR on market share, mortality, and patient mix outcomes associated with CABG demonstrated some evidence that PPR reduces mortality rates in CABG [12▪▪]. An analysis of risk-adjusted CABG outcomes of 39 400 patients in Massachusetts from 2003 to 2014, a mandatory public reporting state, revealed superior results compared with the Society of Thoracic Surgeons National Database data [13]. In light of controversial unintended consequences of public reporting such as risk aversion and denial of care to high-risk patients, further efforts need to be invested in implementing PPR systems throughout the world – either voluntarily or mandatory.

OPERATIVE TECHNIQUES

The CABG procedure is traditionally carried out by use of cardiopulmonary bypass (CPB) (on-pump CABG) and is currently the most preferred technique in the Western world rather than in developing countries in Asia due to high procedural cost associated with cardiopulmonary bypass (CPB) [14,15]. The concept of CABG without the utilization of CPB (off-pump coronary artery bypass; OPCAB) to circumvent deleterious effects associated with CPB have been reported as early as in the 1970s by Trapp and Ankeney with favorable outcomes [16,17]. As such, avoiding aortic cross clamping in particular by anaortic techniques (e.g., in-situ or composite Y-/T-grafting) without manipulation of the ascending aorta or by minimal manipulation using the Heartstring system (Maquet Cardiovascular, San Jose, California) contributed largely to the reduced incidence of stroke after OPCAB in patients with high risk of stroke [18,19]. Although OPCAB procedures were performed with high enthusiasm in the subsequent years, the strong body of evidence derived from large randomized clinical trials (RCTs) has only been provided in this decade. However, in the hand of inexperienced surgeons, OPCAB is associated with inferior early and late graft patency rates, possibly compromising long-term survival. Gaudino *et al.* [20] demonstrated surgeons' inexperience with the OPCAB procedure to be associated with increased mortality. In-line with this finding, Benedetto *et al.* [21▪▪] further highlighted

a volume-based dependency of outcomes in OPCAB surgery in a retrospective analysis of the Nationwide Inpatient Sample database including a total of 2094 094 patients undergoing on-pump and off-pump coronary artery bypass surgery.

Associated mortality of OPCAB procedures performed in high-volume off-pump CABG centers (≥164 cases per year) and by experienced surgeons (≥48 cases per year) was reduced compared with on-pump coronary artery bypass grafting with two or more grafts [21▪▪]. Not only these observations stimulated Mack and Taggart to propose CABG surgery to be a subspecialty within cardiac surgery [22▪▪]. Not surprisingly, Watkins *et al.* [23▪▪] observed an improvement of survival after implementation of a dedicated subspecialized CABG program in a retrospective, single-center analysis. In light of recent developments in cardiac surgery with multidisciplinary heart teams of specialists and specific expertise dedicated to heart failure therapies (transplant, mechanical circulatory support), mitral valve therapies, aortic valve therapies and thoracic aortic therapies, this proposal seems highly justified and may shape the upcoming future of surgical coronary revascularization.

MINIMALLY INVASIVE APPROACHES

The momentum gained by catheter-based aortic and mitral valve therapies driven by the desire of patients for lesser invasiveness and faster recovery is undeniable. This trend cannot and is not ignored for CABG surgery and is expected – with further improvements – to be the mainstay of future surgical coronary revascularization strategies. As such, in an effort to mitigate the invasiveness of CABG by avoiding open sternotomy, minimally invasive direct CABG (MIDCAB) with grafting of the left internal mammary artery (LIMA) to the left anterior descending (LAD) in off-pump technique through a limited-access minithoracotomy emerged in the 1990s as a promising alternative. However, this access is not limited to single anastomosis and total arterial revascularization using composite bilateral internal mammary artery (BIMA)-Y-conduits was not only shown to be feasible but a safe and reproducible procedure with excellent midterm outcomes [24,25▪▪]. The Minimally Invasive coronary surgery compared with STernotomy coronary artery bypass grafting (MIST) trial, a multicentre, prospective, open label, randomized control trial aims to compare quality of life and recovery in the early postoperative period, between patients with multivessel CAD undergoing CABG by minimally invasive approach versus sternotomy. The trial has started in 2018 with an anticipated randomization of 88 patients for each group and is currently enrolling [26].

Another approach emerged by integrating PCI for non-LAD territories with simultaneous or sequential MIDCAB as hybrid coronary revascularization (HCR). Further refinements include video-assisted or robotic-assisted harvesting of the LIMA graft. Despite encouraging results mainly published from retrospective single-center studies with short-term follow-up (FU) and rather small sample sizes, evidence for HCR remains limited and hypothesis generating [27–29]. In one of the few RCTs, the 5-year clinical follow-up of the HYBRID (Hybrid Revascularization for Multivessel Coronary Artery Disease) trial with a total of 200 patients randomly assigned to undergo HCR or conventional CABG showed similar 5-year all-cause mortality when compared with conventional CABG [30]. The Hybrid Coronary Revascularization Trial (ClinicalTrials.gov Identifier: NCT03089398), a prospective, multicenter randomized comparative effectiveness trial of HCR compared with multivessel PCI with drug-eluting stents in patients with multivessel CAD involving the LAD or left main territories with an anticipated enrollment of 2354 patients was expected to provide robust evidence from a large-scale RCT in support for HCR. However, due to slow enrollment, this trial was stopped early after only 200 patients were randomized.

A further evolution of minimally invasive techniques involves robot-assisted totally endoscopic grafting of the LIMA–LAD anastomosis as part of HCR as well as multiple bypass grafting in totally endoscopic coronary bypass grafting (TECAB) with the aid of highly sophisticated telemanipulation systems. Several groups reported on the safety and feasibility of TECAB procedures with outcomes comparable with open CABG procedures [31,32,33▪,34]. However, achievement of high-level-specific skills is mandatory and requires intense training in robotic techniques. Despite incremental improvements in robotic techniques and equipment, devices facilitating anastomosis (distal anastomotic-connectors/coupling devices) thus alleviating the complexity of the procedure still needs further attention. Midterm results of the Multicenter Assessment of Grafts in Coronaries (MAGIC) study demonstrated the commercially available C-Port distal anastomotic device to be safe and effective in creating the distal anastomosis with equivalent patency rates and a statistically significant reduction in midterm graft occlusion to hand-sewn grafts at 12 months [35▪▪]. Meanwhile adoption of this technique remains in dedicated centers, restricted to very few highly specialized surgeons.

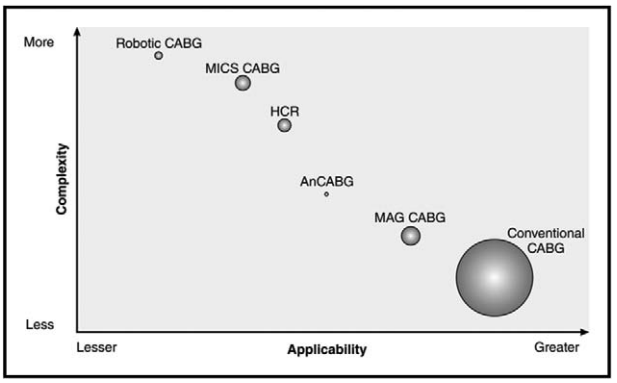

FIGURE 1. Applicability in comparison with complexity of various coronary artery bypass grafting techniques. The size of the circle is proportional to the number of articles published for each technique up to June 2018. AnCABG, anaortic coronary artery bypass surgery; CABG, coronary artery bypass surgery; HCR, hybrid coronary revascularization; MICS, minimally invasive coronary surgery; MAG, multiarterial grafting. Reproduced from Gaudino M, Bakaeen F, Davierwala P, *et al.* New strategies for surgical myocardial revascularization. Circulation 2018;138(19):2160–8.

However, a new Excimer laser-assisted nonocclusive anastomosis-based coronary connector, facilitating sutureless bypass grafting has been recently developed and is currently in preclinical investigation with promising short-term results [36]. Clinical introduction in a pilot study is expected upon completion of long-term safety evaluations in porcine models. The technique has been previously implemented in neurosurgical intracranial-to-intracranial or intracranial-to-extracranial bypasses with promising safety and efficacy results [37]. As to whether a translation into cardiac surgery is feasible remains to be seen. Certainly, any new technology capable of facilitating a safe and durable anastomosis may be the game changer in robotic CABG surgery in the upcoming decades.

Figure 1 illustrates applicability in comparison with complexity of various CABG techniques.

CHOICE OF CONDUIT

While grafting of LIMA to LAD is currently an established approach in CABG surgery due to its proven excellent patency rates with improved survival and freedom from adverse cardiac events, the conduit of choice for non-LAD lesions remains the matter of a heated debate in the cardiovascular community [38]. Traditionally, utilization of the saphenous vein graft (SVG) is common in CABG surgery but due to vein graft disease/failure (VGD/F) with graft-occlusion rates of 40–50% after 10 years, its application has been challenged in the last decades. As such, utilization of the right internal mammary artery, the radial artery (RA) and the right gastroepiploic artery has been under intensive investigations [39–42]. Despite accumulating evidence for BIMA grafting from large nonrandomized risk-adjusted registry data and meta-analyses and unequivocal recommendations in recent US and European guidelines on myocardial revascularization, today adoption of BIMA grafting in clinical routine remains fairly low due to added technical complexity of the CABG procedure, perceived increased morbidity due to associated deep sternal wound infections and doubts on the long-term survival benefits [2,3,41,43–46]. To address these issues, the large-scale prospective randomized multicenter Arterial Revascularization Trial was initiated more than a decade ago and 10-year results have recently been published [47▪▪]. A total of 3102 patients scheduled for CABG were randomly assigned to undergo single ($n = 1545$) or bilateral ($n = 1548$) IMA grafting from June 2004 to December 2007. The primary outcome was defined as death from any cause at 10 years and the secondary outcome as a composite of death from any cause, myocardial infarction (MI), or stroke. A significant between-group difference for the primary and secondary outcome was not observed in the intention-to-treat analysis. The results of this trial with adequate long-term FU may be disappointing for advocates of multiarterial grafting in CABG surgery while opponents may feel vindicated in their reluctance to adopt multiarterial techniques. However, the results of the intention-to-treat-analysis need to be interpreted with caution since a high crossover between groups occurred in the trial. 14% of the patients from the bilateral-graft group eventually received single IMA grafting, and 22% of the patients randomly assigned to the single IMA group received an additional RA graft resulting in multiarterial grafting which is known to result in improved patency and fewer clinical events. The nonrandomized as-treated analysis comparing patients with one single arterial graft and patients with multiarterial grafts however indicated a difference in favor of multiple arterial grafting. The Randomized comparison of the Outcome of Single versus Multiple Arterial grafts (ROMA; ClinicalTrials.gov Identifier: NCT03217006) trial with an anticipated enrolment of 4300 patients started recruitment last year and may provide with a more strict methodology further insight on multiarterial grafting and impact future grafting approaches.

As for another arterial graft, the radial artery has been shown to offer superior patency rates compared with SVGs, yet a recent patient-level combined analysis of randomized, controlled trials performed by

The Radial Artery Database International Alliance investigators failed to demonstrate a significant survival benefit despite superior patency of the RA graft compared with SVGs [48▪,49].

Meanwhile, significant efforts have been invested in addressing the high failure rates of SVGs. The concepts of applying venous external stents, no-touch SVG harvesting techniques and storage of veins after harvesting in dedicated preservation solutions together with high adoption rates of optimized medical therapy post-CABG may further reduce the occurrence of VGD/F and impact the future of conduit choice in CABG surgery [50▪▪,51–53]. The most recent Randomized Trial of Endoscopic or Open Vein-Graft Harvesting for Coronary-Artery Bypass (REGROUP) trial demonstrated no significant difference between open vein-graft harvesting and endoscopic vein-graft harvesting in the occurrence of major adverse cardiac events [54▪▪]. With the drive for lesser invasiveness, a wider adoption in future clinical practice is expected and inevitable.

NEW DIAGNOSTIC TOOLS AND GUIDANCE IN CORONARY ARTERY BYPASS GRAFTING SURGERY

Noninvasive coronary computed tomography angiography (CCTA) performed on modern high-resolution, multidetector scanners with high sensitivity (95–99%) and increasing specificity (64–83%) may represent an interesting alternative to and challenge standard invasive coronary angiography in the diagnosis of CAD. Results of the SYNTAX III REVOLUTION trial demonstrated that in patients with left main or three-vessel disease a heart team treatment decision-making based on CCTA showed high agreement with the decision derived from conventional coronary angiography indicating noninferiority of CCTA compared with invasive angiography [55▪▪].

While fraction flow reserve (FFR)-guided percutaneous revascularization strategies have shown to improve long-term outcomes, equivalent data on the impact of FFR guidance in CABG surgery remains limited [56,57]. In a retrospective analysis of 627 consecutive patients undergoing either angiography-guided or FFR-guided CABG, the rate of overall death or MI was significantly lower in the FFR-guided as compared with the angiography-guided group at up to 6 years of FU [58]. In contrast, a small RCT by Thuesen *et al.* [59] showed similar graft failure rates and clinical outcomes at 6-month FU in 100 patients for FFR-guided and angiography-guided CABG. Interestingly, FFR in deferred lesions was significantly reduced after 6 months and treated subsequently with PCI if the value dropped to less than 0.80 in symptomatic patients. High-quality large-scale RCTs are warranted to evaluate the impact of invasive functionally guided surgical revascularization. As such, the ongoing Graft Patency After FFR-guided versus angiography-guided CABG (GRAFFITI) trial, first of its kind, will provide significant data to optimized graft site selection in surgical revascularization [60▪▪]. Further cardiac imaging technologies in practice and development such as fusion imaging involving anatomical and functional modalities by incorporating CCTA, single photon computed tomography cardiac MRI, and three-dimensional speckle tracking/strain stress echocardiography will significantly improve diagnostic accuracy and guide decision making in future CABG patients (Fig. 2) [61].

PRIMARY AND SECONDARY PREVENTION, PREHABILITATION

The latest 5-year results from the open-label, multicenter, parallel-group SCOT-HEART trial demonstrated that the use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or nonfatal MI at 5 years than standard care alone [62▪]. The investigators attributed this observation to changes of planned investigations and treatments along with increased adherence to primary prevention medications during the FU period. Not only primary, but also secondary prevention measures play a crucial role in the management of CABG patients by improved survival [63].

As such, suboptimal medical management in CABG as shown in many randomized trials needs further optimization by means of adopting recent guidelines recommendations [63,64]. To further improve outcomes in CABG, recent trends of preoperative conditioning by means of improving the functional capacity through multimodal prehabilitation (preoperative rehabilitation) programs need further attention [65].

CONCLUSION

CABG surgery evolved in incremental but significant steps since its introduction. The fate of surgical coronary revascularization in 25 years will mainly be determined by the adequate incorporation of present techniques, choice of grafts and patient selection and decision making based on individual patient risks as well as wider adoption of available minimally invasive techniques. Subspecializing CABG within cardiac surgery by any means of technique seems inevitable and requires intense structured training in highly dedicated programs. The search for the second best conduit remains in

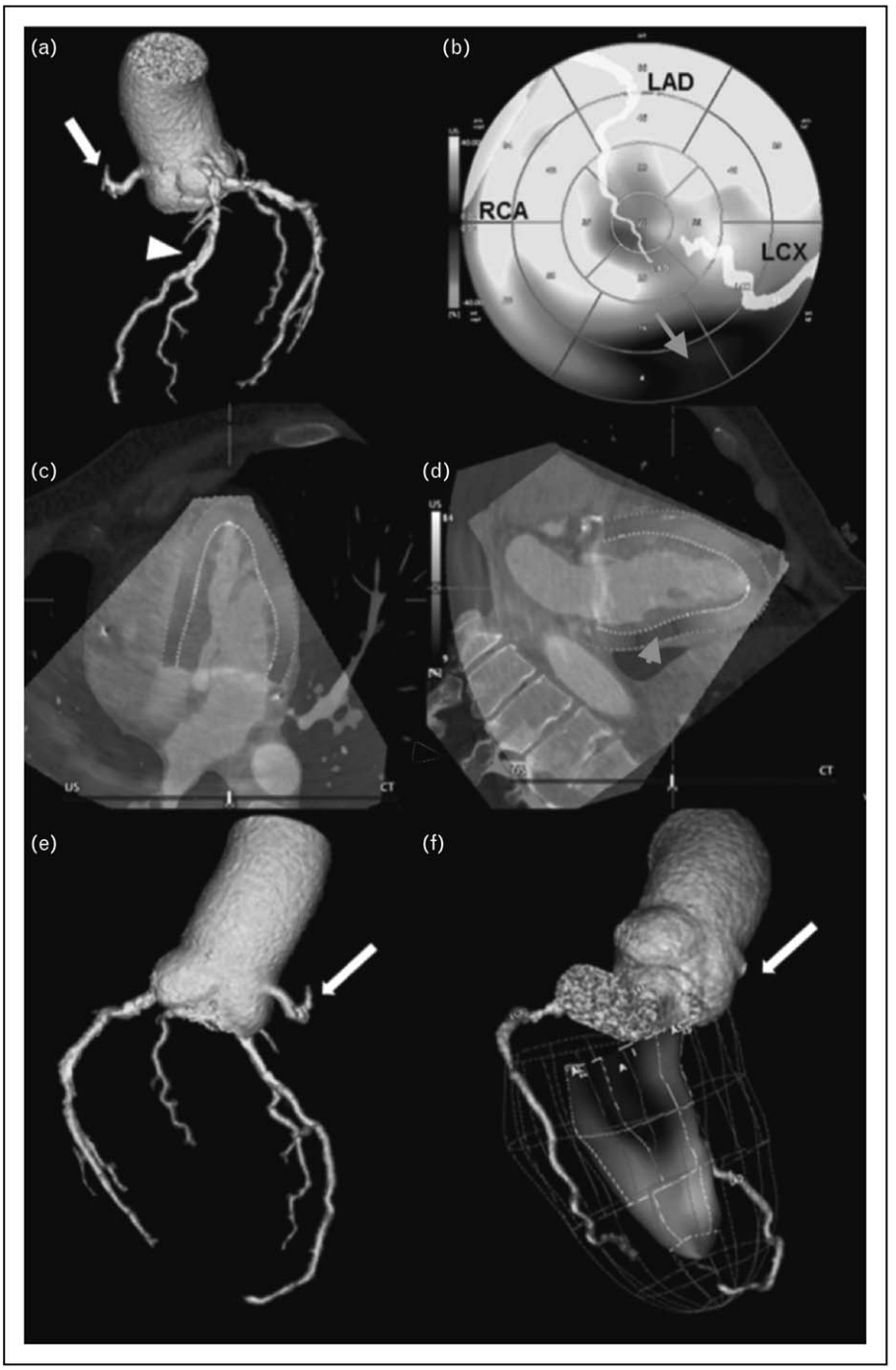

FIGURE 2. Cardiac hybrid imaging combining three-dimensional echocardiography and coronary computed tomography angiography allows assessing comprehensive anatomic and functional information at the same time. Chronic total occlusion of the right coronary artery (panel a, arrow) and a calcified intermediate stenosis of the left anterior descending artery (panel a, arrowhead). Wall motion abnormality in the inferior segments as well as a small area in the apical region depicted by polar mode in three-dimensional-strain imaging (panel b, grey-scaled arrow). Anatomical matching between the three-dimensional strain dataset and the main coronary arteries from three-dimensional coronary computed tomography angiography dataset based on size and orientation from coronary computed tomography angiography (panels c and d). The coronary tree with superimposed three-dimensional strain dataset (panel e and f) indicating that the large ischemic region (grey-scaled arrowhead) is subtended by the right coronary artery (arrow), while the small, prognostically nonrelevant ischemic region is subtended by the left anterior descending. Reproduced from [61].

progress and will highly affect outcomes in patients with CAD progressively presenting in younger patients. Available and upcoming diagnostic tools such as CCTA, FFR or instantaneous wave-free ratio need further attention and may contribute significantly in the patient selection and decision making process. Efforts of reducing the invasiveness of the procedure should remain in the focus but without a breakthrough of technologies robotic coronary surgery will be forced to carve a niche existence in the hands of highly specialized centers and surgeons.

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Conflicts of interest

There are no conflicts of interest.

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